REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Claims 14, 15, 17, 18 and 20 have been amended editorially. No new matter has been added. Claims 11-20 are pending. Applicant respectfully requests entry and consideration of the amendments.

Priority

Applicants respectfully submit that a submission of a certified copy of the Chinese priority application is not necessary in a US national stage filing. Applicants respectfully request acknowledgment of priority of this PCT National Stage application.

Claim Rejections- 35 U.S.C. 101/112

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Claim 14 has been amended, taking the issues noted in the rejection into account. In particular, the pH adjusting step after the oxidation degradation reaction has been removed. Applicants submit that claim 14 and its dependent claims comply with the written description requirement.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Claim 18 has been amended, taking the issues noted in the rejection into account. In particular, claim 18 has been amended to recite a method for the prophylaxis or treatment of Alzheimer's disease or diabetes. Applicants submit that claim 18 recites an active step.

Claim 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use results in an improper definition of a process. Claim 18 has been amended, taking the issues noted into account. Claim 18 is directed to a method, and recites the step of administering an effective amount of mannuronic acid oligosaccharide represented by the formula I to a mammal. Applicants submit that claim 18 recites a proper process.

Claim Rejections- 35 U.S.C. 102

Claims 11-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Yang et al. (Carbohyd. Polym., 2004).

Filed herewith is a verified translation of the present Chinese priority application CN 200410023827.0 filed March 24, 2004. CN 200410023827.0 describes the chemical structure and also refers to Application number 03138976.7, which discloses the claimed structure that distinguishes it from other materials. Accordingly, there is a reasonable basis to conclude that the priority application has disclosure to show that the Applicants were in possession of the claimed subject matter at the time the present Chinese priority application was filed. The March 24, 2004 date is earlier than the publication date of Yang et al. Therefore, Yang et al. is not available as prior art and the rejection should be withdrawn. Applicants do not concede the correctness of the rejection.

Claims 11-13, 19 and 20 are rejected under 35 USC 102(b) as being anticipated by Marritt (US 2002/0016453). Applicants respectfully traverse the rejection.

Claim 11 is directed to an alginate oligosaccharide derivative or their pharmaceutically-acceptable salts. The alginate oligosaccharide derivatives are composed of β-D-mannuronic acid linked by 1,4 glycosidic bonds, where the reduced terminal in position 1 is carboxyl radical as shown in the formula II.

The rejection recognizes that Marritt is silent as to the oxidation level of the reducing end of the oligosaccharide, but refers to paragraphs [0009]-[0017], [0061]-[0068] and Example 3 of Marritt, and contends that it would be expected that the product would be identical to the one of formula II of claim 11 since the processing was accomplished with an oxidant. Applicants respectfully submit that the aliginate oligosaccharide derivate of claim 11 cannot be obtained by the preparations disclosed by Marritt.

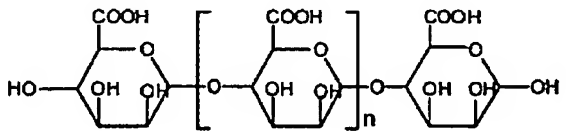
In particular, Marritt teaches the use of Fenton's reagent, i.e., a combination of hydrogen peroxide and iron salt, for the oxidative degradation of the polyuronic acids (see paragraphs [0013], [0021], [0064], and [0091]). Example 3 of Marritt provides the preparation of polymannuronic acid using Fenton's reagent and the characterization of the obtained product. In Example 3, the internal peaks in H-1, H-2, H-4, H-3 and H-5 are provided for the obtained product, but it cannot be determined from this disclosure as to

whether the obtained product was oxidated to a carboxyl group from an aldehyde group on the reduced terminal in position 1. That is, if the reduced terminal in position 1 is an aldehyde group, the chemical shift of H-1(α) should be around 5.11 ppm and the chemical shift of H-1(β) should be around 4.81 ppm (see page 9 under 4.3 ^{1}H-NMR analysis of the present specification; see also Table 1 on page 15 of Heyraud et al., Carbohydrate Research, 289 (1996); for the Examiner's convenience, a copy of the Heyraud reference is submitted herewith). Marritt does not provide this data.

The rejection notes that the burden is on the Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. Applicants hereby submit a Rule 1.132 Declaration by one of the inventors, Dr. Meiyu Geng. The Rule 1.132 Declaration includes experimental work to demonstrate that the product of claim 11 does not correspond to the product of Marritt, and further, that the product of claim 11 cannot be obtained by the method disclosed by Marritt.

Briefly, polymannuronic acid was prepared as in Example 3 of Maritt. In particular, polymannuronic acid was dissolved in lithium salt, and treated with Fenton's reagent, that is, hydrogen peroxide and a ferrous salt (ferrous sulfate heptahydrate). After the reaction was stopped, the solid was collected, filtered, washed and dried. The mannuronate oligosaacharides degraded from polymannuronate were then size separated. 4-mer of the obtained product was then subjected to Mass Spectrum analysis and ^{1}H-NMR analysis to show the characterization of its structure.

As indicated on page 4 of the Declaration, MS analysis showed that the molecular weight of the 4-mer was 722, which corresponds to the 4-mer having the following structure:



Moreover, as indicated on pages 4-5 of the Declaration, the 4-mer exhibited chemical shifts H1, H2, H3, H4 and H5 that corresponded to that of Marritt, thereby indicating that the 4-mer corresponds to Marritt's product. Significantly, the 4-mer also exhibited a chemical shift of H-1(α) at 5.21 ppm and a chemical shift of H-1(β) at 4.91 ppm, thereby

indicating that the reduced terminal in terminal position 1 of the alignate oligosaccharide was not oxidated to a carboxyl group from the aldehyde group. Even further, under ^{13}C-NMR spectrum analysis, the 4-mer exhibited a chemical shift of C-1 at the reducing end at 94 ppm (C-1rα at 93.54 and C-1rβ at 93.74 ppm), thereby further confirming that the alignate oligosaccharide was not oxidated to a carboxyl group from the aldehyde group (the reported chemical shift of C-1r is about 94 rpm; see Table 3 of Heyraud et al.).

On the other hand, the alginate oligosaccharide derivatives of claim 11 is obtained by using a completely different degradation agent, namely $Cu(OH)_2$, so as to obtain a completely different product. As shown on page 9 of the specification, ^1H-NMR analysis of the alginate oligosaccharide derivatives of claim 11 resulted in the disappearance of the signals at 5.11 ppm and 4.81 ppm, thereby indicating that the reduced terminal position in position 1 of the alginate oligosaccharide derivative of claim 11 was oxidated to a carboxyl group from an aldehyde group. This was further confirmed with ^{13}C-NMR analysis, where the signal of the reduced terminal C-1 at 94 ppm disappeared. Even further, as indicated on page 10 of the present specification, Mass Spectrum analysis also confirmed that the alginate oligosaccharide derivative of claim 11 was oxidated during its preparation.

It is clear from the experimental work of the present specification and the work described in the Declaration that the polymannuronic acid of Marritt does not correspond to the alginate oligosaccharide derivatives of claim 11, and that the alginate oligosaccharide derivatives of claim 11 cannot be obtained by the methods disclosed by Marritt. Nothing in Marritt teaches or even suggests the alginate oligosaccharide derivatives of claim 11. Accordingly, claim 11 and its dependent claims are patentable over Marritt.

S/N 10/594100 PATENT

In view of the above amendments and remarks, Applicant believes that the pending claims are in a condition for allowance. Favorable reconsideration is respectfully requested. If any questions arise regarding this communication, the Examiner is invited to contact Applicant's representative listed below.

Respectfully submitted,

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